PLANT GROWTH REGULATORS

Synthesis and Preliminary Evaluations of Amide, Lactic Acid, and Terpenoid Derivatives of Substituted Phenoxycarboxylic Acids

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These investigations were undertaken for the purpose of utilizing materials of agricultural origin in the synthesis of conjugated biologically active compounds. All of the 32 new compounds prepared, amides, terpenoids, and lactic acid derivatives, induced plant-growth responses. In general, the magnitude of these responses was less than that induced by the parent regulating compounds. The data presented indicate that some derivatives may possess limited growth-regulating properties of interest inducing a localized response. In a few cases the coupling of compounds with halogenated phenoxy acids produced derivatives possessing increased growth-regulating properties.

THE SYNTHESIS and preliminary evaluation of biologically active compounds have been reported in a series of papers (*7–9*, *13*, *14*). The broad purpose of the work is to create new and useful, synthetically prepared compounds from naturally occurring and derived source materials of agricultural origin. These investigations are motivated by the desire to obtain fundamental knowledge on the mode of action of growth regulators in plant metabolism and the effects of modification of chemical structure on the biological activity of plant growth substances. The immediate objective is the preparation of plant growth-regulating compounds possessing significantly different growth-regulating properties from those of parent substances holding prominence in the "growth regulator" field. Some of the desirable attributes sought are increased or decreased selectivity and translocatibility, modified phytotoxicity, and new growth-regulating properties.

This publication is a report on the preparation and some plant-regulating effects obtained with *p*-toluenesulfonamide (included because of chemical similarity to several naturally occurring amino acids), *p*-aminobenzoic acid, *p*-aminosalicylic acid, and several lactic acid derivatives of halogenated phenoxycarboxylic acids; it also includes results of a preliminary evaluation of new derivatives of the terpenoids: nopol 1-[6,6-dimethylbicyclo-(1,1,3)-hept-2-en-2-yl]-ethan-2-ol (*1*), hydronopol, and Terposol No. 8 (chiefly terpinyl ethylene glycol ether).

The part reported here on amide derivatives is an extension of previous studies (*7–9*, *14*) which have demonstrated that amino acid coupling can have a marked effect upon the growth-regulating properties of a compound. This type of coupling has also resulted in an increase in the selectivity of the phenoxy-type growth regulator. Work on other amino acid, peptide, and protein hydrolyzate derivatives is in progress. Need for extended work covering a wide variety of terpenoids is indicated by the results obtained here and by others in the field of weed control (*2*, *4*). New inexpensive terpenoids used as starting ma-

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Table I. Physical Properties, Yields, and Analytical Data for Halogenated Phenoxy Acyl Chlorides

Name	Formula	Boiling Point, ° C. (Uncor.)	Melting Point, ° C. (Uncor.)	n_{D}^{25}	Yield, %	Analyses, %					
						Carbon		Hydrogen		Chlorine	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
4-Chlorophenoxyacetyl chloride[a]	$C_8H_6Cl_2O_2$	92.0/1.0 mm.	22.0–24.0	1.5463	85.0	46.86	47.07	2.95	3.04	34.85	35.40
2-Methyl-4-chlorophenoxyacetyl chloride	$C_9H_8Cl_2O_2$	70.0/0.007 mm.	28.5–30.0	1.5400[b]	93.5	49.34	50.04	3.68	4.17	32.37	32.56
2,4-Dichlorophenoxyacetyl chloride[c]	$C_8H_5Cl_3O_2$	102–105/0.3 mm.	50.3–52.3[d]	1.5622	87.8	40.13	40.22	2.11	1.90	44.42	44.30
2,4,5-Trichlorophenoxyacetyl chloride[e]	$C_8H_4Cl_4O_2$	128–130/2.0 mm.	84.5–85.0[d]	1.5590[f]	74.2	35.08	35.25	1.47	1.81	51.76	51.68
2-(2,4-Dichlorophenoxy)propionyl chloride[g]	$C_9H_7Cl_3O_2$	76.0/0.1 mm.	...[h]	1.5440	90.4	42.59	43.25	2.74	3.23	41.96	41.97
2-(2,4,5-Trichlorophenoxy)propionyl chloride	$C_9H_6Cl_4O_2$	111–117/0.3 mm.	...[h]	1.5601[i]	73.0	37.54	37.73	2.10	2.23	49.25	48.96
4-(2,4-Dichlorophenoxy)butyryl chloride	$C_{10}H_9Cl_3O_2$	136–140/0.2 mm.	17.0–22.0	1.5465	89.1	44.89	44.93	3.39	3.38	39.76	39.43
4-(2-Methyl-4-chlorophenoxy)butyryl chloride	$C_{11}H_{12}Cl_2O_2$	115–122/0.2 mm.	5.0–9.0	1.5340	73.5	53.46	53.45	4.90	5.19	28.70	28.62

[a] B.p. 142°/17 mm., m.p. 18.8, yield 90% (*10*).
[b] At 32.8° C.
[c] B.p. 155–157°/22 mm., yield 84–90% (*14*).
[d] Cor.
[e] B.p. 165–167°/6 mm., m.p. 78–79°, yield 80% (*6*).
[f] At 94° C.
[g] B.p. 137–139°/9 mm., n_{D}^{20} = 1.5475, yield 84% (*5*).
[h] Liquid at 5° C.
[i] At 26.0° C.

Table II. Physical Properties, Yields, and Analytical Data for Amide Derivatives of Halogenated Phenoxy Acids

Name	Formula	M.P., °C.[a] (Cor.)	Yield				Analyses, %			
			Crude		Refined		Chlorine		Nitrogen	
			G	%	G	%	Calcd.	Found	Calcd.	Found
p-Toluenesulfonamide										
N-(4-chlorophenoxyacetyl)-	$C_{15}H_{14}ClNO_4S$	169–171	4.37	64.2	1.72	25.3	10.43	10.54	4.12	4.02
N-(2-methyl-4-chlorophenoxyacetyl)-	$C_{16}H_{16}ClNO_4S$	204–206	5.34	75.3	2.20	28.5	10.02	9.93	3.96	3.96
N-(2,4-dichlorophenoxyacetyl)-	$C_{15}H_{13}Cl_2NO_4S$	170–171	3.96	52.7	2.75	36.6	18.96	18.99	3.75	3.75
N-(2,4,5-trichlorophenoxyacetyl)-	$C_{15}H_{12}Cl_3NO_4S$	177–179	6.48	79.4	3.35	41.0	26.03	25.74	3.43	3.45
N-[DL-2-(2,4-dichlorophenoxy)propionyl]-	$C_{16}H_{15}Cl_2NO_4S$	123–125	4.78	63.8	1.35	18.0	18.29	18.12	3.61	3.51
Aminobenzoic acid										
N-(4-chlorophenoxyacetyl)-	$C_{15}H_{12}ClNO_4$	237–239	4.10	66.9	3.85	62.8	11.59	11.92	4.58	4.63
N-(2-methyl-4-chlorophenoxyacetyl)-	$C_{16}H_{14}ClNO_4$	260–263[b]	3.30	51.6	2.78	43.5	11.09	11.17	4.38	4.39
N-(2,4-dichlorophenoxyacetyl)-	$C_{15}H_{11}Cl_2NO_4$	272–275	3.02	83.6	2.30	64.1	20.55	20.70	4.11	4.13
N-(2,4,5-trichlorophenoxyacetyl)-	$C_{15}H_{10}Cl_3NO_4$	310–315[c]	...	...	1.13[d]	15.1	28.39	27.99	3.74	3.72
N-[DL-2-(2,4-dichlorophenoxy)propionyl]-	$C_{16}H_{13}Cl_2NO_4$	208–209[b]	14.18	100.0	6.13	44.5	20.02	20.02	3.96	3.99
p-Aminosalicylic acid										
N-(4-chlorophenoxyacetyl)-	$C_{15}H_{12}ClNO_5$	225–227	4.32	67.0	1.95	30.2	11.02	11.12	4.37	4.36
N-(2-methyl-4-chlorophenoxyacetyl)-	$C_{16}H_{14}ClNO_5$	223–227[e]	...	...	1.68	25.0	10.54	10.56	4.21	4.17
N-(2,4-dichlorophenoxyacetyl)-	$C_{15}H_{11}Cl_2NO_5$	256–258	4.92	68.9	1.55	21.7	19.90	19.40	3.92	3.84
N-(2,4,5-trichlorophenoxyacetyl)-	$C_{15}H_{10}Cl_3NO_5$	281–284[b]	...	...	2.07	26.5	27.23	27.02	3.59	3.54
N-[DL-2-(2,4-dichlorophenoxy)propionyl]-	$C_{16}H_{13}Cl_2NO_5$	215–221	3.81	51.4	2.91	39.3	19.16	19.07	3.78	3.79

[a] Recrystallized once or more from ethyl alcohol water and ethyl acetate–petroleum ether unless otherwise indicated.
[b] Recrystallized from ethyl alcohol water only.
[c] Recrystallized from ethyl alcohol water and ethylene glycol monoethyl ether.
[d] A portion of sample lost by accident.
[e] Recrystallized twice from methanol water.

Table III. Physical Properties, Yields, and Analytical Data for Lactic Acid Derivatives of Halogenated Phenoxy Acids

Name	Formula	Boiling Range, ° C. (Uncor.)	n_D^{25}	d_4^{25}	Yield, %		Analyses, %					
					Crude	Refined	Carbon		Hydrogen		Chlorine	
							Calcd.	Found	Calcd.	Found	Calcd.	Found
DL-2-[DL-2-(2,4,5-trichlorophenoxy)propionoxy] propionic acid methyl ester[a]	$C_{13}H_{13}Cl_3O_5$	170–90/0.2mm.	1.5232	1.3649	78	66	43.91	44.41	3.68	3.82	29.91	29.59
DL-2-[DL-2-(2,4,5-trichlorophenoxy) propionoxy] propionic acid *n*-butyl ester	$C_{16}H_{19}Cl_3O_5$	187–93/0.2 mm.	1.5094	1.2679	..	75	48.32	48.53	4.82	4.92	26.75	26.30
DL-2-(2-methyl-4-chlorophenoxy acetoxy)propionic acid methyl ester	$C_{13}H_{15}ClO_5$	167–75/0.2 mm.	1.5077	1.2340	..	65	54.46	54.38	5.27	5.16	12.37	12.69
DL-2-(2-methyl-4-chlorophenoxy acetoxy)propionic acid *n*-butyl ester	$C_{16}H_{21}ClO_5$	190–205/0.2 mm.	1.4954	1.1520	69	53	58.45	58.00	6.44	6.05	10.78	10.99
									Nitrogen			
DL-2-(2,4-dichlorophenoxyacetoxy)propionic acid *N*-ethylamide	$C_{13}H_{15}Cl_2NO_4$	108.5–9.5 (m.p. cor.)	......	......	21	12	.....	.....	4.37	4.47	22.15	22.18

[a] Solidified to soft waxy crystals.

terials are being supplied by the Naval Stores Section of the Agricultural Research Service's Southern Regional Research Laboratory. The chemistry on the preparation and purification of the terpenoid derivatives used in the present experiments has been reserved for publication with extended studies now in progress on volatility and herbicidal properties.

The development of "lactoprene" rubbers at the Eastern Regional Research Laboratory made available a wide variety of lactic acid derivatives for synthetic purposes. Attempts in 1953 to couple lactic acid and some of its derivatives with halogenated phenoxycarboxylic acids were unsuccessful. However, a single compound, DL-2-(2,4-dichlorophenoxyacetoxy)propionic acid *N*-ethylamide, combining DL-*N*-ethyllactamide with 2,4-dichlorophenoxyacetic acid, was made and preliminary tests showed that it possessed growth-regulating properties; also it was quick-acting on the test plants used. A discovery made about this time (*11*) that leaves of test plants (corn was an exception) were able to translocate plant regulating carbamates more readily when the compounds contain the lactic acid group kept alive the desire to incorporate lactic acid into the phenoxy type regulator. Four more lactic acid derivatives have now been made and a preliminary evaluation of all five compounds is reported here.

Experimental

Compounds used for synthetic purposes were the best obtainable from commercial sources, utilized without further purification. Where new derivatives prepared were solids, no attempts were made to improve yields by working up mother liquors.

For the preparation of the amide derivatives of halogenated phenoxycarboxylic acids obtained by coupling *p*-toluenesulfonamide, *p*-aminosalicylic acid, and *p*-aminobenzoic acid Schotten-Baumann techniques were used (*7–9*). When it was necessary, halogenated phenoxycarboxylic acids were first converted to their acyl chlorides by the use of thionyl chloride employing the method of Freed (*3*). Informative data concerning the properties of all the chlorides used are summarized in Table I. Values obtained by other investigators are also presented. Data on 4-(2,4-dichlorophenoxy)butyryl and 4-(2-methyl-4-chlorophenoxy)butyryl chlorides are included, because these compounds have been used to prepare amino acid derivatives which are being evaluated as herbicides.

The preparation of 2,4,5-trichlorophenoxyacetyl-*p*-toluenesulfonamide is illustrative of that used for the other sulfonamides and for the derivatives of *p*-aminobenzoic and *p*-aminosalicylic acids. Melting points, yields, and analytical data for these compounds are recorded in Table II.

2,4,5-Trichlorophenoxyacetyl-*p*-toluenesulfonamide. To *p*-toluenesulfonamide (3.42 grams, 0.02*M*) dissolved in 60 ml. of 1*N* sodium hydroxide chilled to 5° C. was added, dropwise with continuous stirring, a cold solution containing 2,4,5-trichlorophenoxyacetyl chloride (5.46 grams, 0.02*M*) dissolved in 30 ml. of benzene. The reaction mixture was stirred for 3 hours as it warmed to room temperature. Three 20-ml. portions of ether were used for extractions made in a separatory funnel. The combined ether extracts were washed with 20 ml. of distilled water. The washing was returned to the alkaline solution, which was then acidified with 1*N* hydrochloric acid using Congo red paper as an indicator. The acidified solution was placed in the refrigerator overnight. The white crystalline product was filtered off, slurried three times with water, and finally dried in a vacuum desiccator by continuous overnight pumping. The product was ground and washed three times with small portions of warm petroleum ether (boiling range 63° to 70° C.). The crude yield was 6.48 grams (79.4%), melting point 165–70° C. Following two recrystallizations by dissolving in hot ethyl acetate and precipitating with petroleum ether the melting point was 174–9° C.

A third recrystallization performed by dissolving in hot ethyl alcohol and precipitating with water produced a product with a satisfactory melting point, 177 to 179° C. The final yield was 3.35 grams (41.0%) (Table II).

The lactic acid derivatives were prepared by two varying techniques. First the *n*-ethylamide of DL-2-(2,4-dichlorophenoxyacetoxy) propionic acid was made by the azeotropic technique.

DL-2-(2,4-Dichlorophenoxyacetoxy) propionic Acid *N*-Ethylamide. DL-*N*-Ethyllactamide (*12*) (78.0 grams,

Table IV. Plant Growth-Regulating Activity of Amide, Lactic Acid, and Terpenoid Derivatives of Halogenated Phenoxy Acids on Black Valentine Bean (*VB*), Sunflower (*S*), Cucumber (*C*), Barley (*B*), and Corn (*Cn*)^a

	Lanolin Method																					Coated Sand Method			
													Cell Proliferation												
	Stem Curvature			Growth Inhibition			Epinasty			Formative Effects			First Internode			Hypocotyl			Treated Area			Stem Curvature		Growth Inhibition	
Compounds Tested	VB	S	C	VB	S	C	VB	S	C	VB	S	C	VB	S	C	VB	S	C	VB	S	C	B	Cn	B	Cn
Parent acids																									
4-Chlorophenoxyacetic	1^b	0^b	3^b	3^b	3^b	3^b	0^b	0^b	2^b	1^b	2^b	3^c	2^b	0^b	0^b	0^b	0^b	0^b	3^b	0^b	0^b	0	0	3	0
2-Methyl-4-chlorophenoxyacetic	3	3	3	2	3	3	0	3	3	0^b	0^b	0^c	3	0	0	3	0	0	3	3	0	1	3	2	1
2,4-Dichlorophenoxyacetic	1^b	1^b	3^b	3^b	3^b	3^b	0^b	1^b	3^b	0^b	2^b	2^c	0^b	0^b	0^b	1^b	0^b	0^b	3^b	0^b	1^b	3	3	0	3
2,4,5-Trichlorophenoxyacetic	0	2^b	3^b	3	3	3	0	2^b	3^b	3^b	3^b	3^c	3	0^b	0^b	3	1^b	0^b	3	1^b	0^b	1	3	3	1
DL-2-(2,4-Dichlorophenoxy) propionic	2^b	1^b	0^b	2^b	2^b	3^b	0^b	0^b	0^b	0^b	1^b	2^b	0^b	0^b	0^b	0^b	1^b	0^b	3^b	1^b	0^b	2	1	3	1
DL-2-(2,4,5-Trichlorophenoxy) propionic	3^b	2^b	3^b	3^b	3^b	3^b	0^b	1^b	3^b	0^b	1^b	2^c	2^b	0^b	0^b	3^b	1^b	0^b	3^b	1^b	0^b				
p-Toluenesulfonamides																									
N-(4-chlorophenoxyacetyl)-	1	3	3	3	3	2	0	3	0	3^b	2^b	3	3	0	0	0	3	1	3	3	3	3	1	2	1
N-(2,methyl-4-chlorophenoxyacetyl)-	0	0	0	2	3	0	0	0	0	1	1	1	0	0	0	0	1	3	3	1	3	2	1	2	1
N-(2,4-dichlorophenoxyacetyl)-	2	3	0	3	3	0	0	0^b	0	2^b	2^b	2	3	0^b	0	3	0^b	0	3	1^b	3	2	2	2	1
N-(2,4,5-trichlorophenoxyacetyl)-	3	0	1	3	3	2	0	0	1	1	1^b	1	3	3	3	3	3	3	3	3	3	1	2	0	0
N-[DL-2-(2,4-dichlorophenoxy) propionyl]-	1	0	0	3	3	3	0	0	0	0^b	0	3^b	3	0	0	0	1	3	3	1	3	1	0	2	0
p-Aminobenzoic acids																									
N-(4-chlorophenoxyacetyl)-	1	1	3	3	2	2	0	2	0	1	0	3	3	2	0	1	1	2	3	2	2	2	0	2	0
N-(2-methyl-4-chlorophenoxyacetyl)-	0	0	3	0	0	2	0	0	1	1	1	0	0	0	0	0	1	2	1	1	2	1	2	2	2
N-(2,4-dichlorophenoxyacetyl)-	0	0	3	2	2	2	0	0	0	3	1	1	0	0	0	0	3	2	2	3	3	2	1	2	1
N-(2,4,5-trichlorophenoxyacetyl)-	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	3	0	0	3	0	1	0	0
N-[DL-2-(2,4-dichlorophenoxy) propionyl]-	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	1	1
p-Aminosalicylic acids																									
N-(4-chlorophenoxyacetyl)-	0	1	3	3	3	3	0	0	3	3	1^b	3^b	3	3	0	0	2	1	3	3	1	0	0	1	0
N-(2-methyl-4-chlorophenoxyacetyl)-	1	1	3	3	3	3	0	2	0	2	2^b	3^b	0	3	0	0	2	3	3	3	3	1	2	1	1
N-(2,4-dichlorophenoxyacetyl)-	1	2	3	2	3	3	0	0	1	3	3	3^b	0	1	0	0	3	1	2	3	1	1	1	2	1
N-(2,4,5-trichlorophenoxyacetyl)-	1	1	3	3	2	3	0	0	3	0^b	2	0	0	0	0	0	2	1	1	2	1	1	1	0	0
N-[DL-2-(2,4-dichlorophenoxy) propionyl]-	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	2	0	0	1	1

Lactic acid derivatives																									
DL-2-[2-DL-(2,4,5-trichlorophenoxy) propionoxy]-propionic acid, methyl ester	3	1	3	3	2	3	0	1	3	0[b]	1	0	2	0	0	2	1	0	2	1	0	0	2	1	0
DL-2-[2-DL-(2,4,5-trichlorophenoxy) propionoxy]-propionic acid, *n*-butyl ester	2	0	1	3	2	2	0	0	1	0	2	0	0	0	0	2	0	1	3	0	1	0	2	0	1
DL-2-(2-methyl-4-chlorophenoxyacetoxy) propionic acid, methyl ester	3	3	2[b]	3	3	3[b]	0	3	3[b]	3[b]	2	2[c]	1	0	0[b]	2	0	0[b]	3	0	0[b]	0	1	1	2
DL-2-(2-methyl-4-chlorophenoxyacetoxy) propionic acid, *n*-butyl ester	3	3	3	3	3	2	0	3	3	0[b]	2	2	0	0	0	1	1	1	2	1	1	0	2	2	2
DL-2-(2,4-dichlorophenoxyacetoxy) propionic acid *N*-ethylamide	2	3	3	3	3	1	0	0	3	0	1	2	0	0	2	2	1	1	3	1	1	3	0	1	0
Parent terpenoid compounds																									
Hydronopol	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nopol	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hydronopyl-																									
4-chlorophenoxyacetate	0	0	3	1	0	3	1	0	0	3	2	3[b]	0	0	0[b]	0	0	0	2	0	0	0	0	2	0
2-methyl-4-chlorophenoxyacetate	0	0	3	1	2	3	0	0	0	0	0	3[b]	0	0	0[b]	0	0	0	2	3	0	0	0	3	2
2,4-dichlorophenoxyacetate	3	0	3	2	3	3	0	0	0	2	0	3[b]	2	0	0[b]	1	0	0	2	2	0	0	0	2	1
2,4,5-trichlorophenoxyacetate	1	0	3	0	2	3	0	0	0	0	0	2[b]	0	0	0[b]	0	1	0	2	3	0	0	0	1	1
DL-2-(2,4-dichlorophenoxy) propionate	0	0	3	1	0	3	0	0	0	0	3	3[b]	0	0	0[b]	0	0	0	1	0	0	0	0	1	2
Nopyl-																									
4-chlorophenoxyacetate	1	0	3	3	3	3	1	0	0	3	3	3[b]	0	0[b]	0[b]	0	0	0	3	0	0	0	0	1	1
2-methyl-4-chlorophenoxyacetate	2	0	3	1	3	3	0	0	0	1	0	3[b]	0	0[b]	0[b]	0	0	0	2	0	0	1	0	2	2
2,4-dichlorophenoxyacetate	2	0	3	3	3	3	0	0	0	1	0	3[b]	2	0[b]	0[b]	2	0	0	3	0	0	0	0	2	2
2,4,5-trichlorophenoxyacetate	1	0	3	2	2	3	0	0	0	0	0	3[b]	1	0[b]	0[b]	1	0	0	2	0	0	1	2	1	1
DL-2-(2,4,dichlorophenoxy) propionate	0	0	3	1	1	3	0	0	0	0	2	2[b]	0	0[b]	0[b]	0	0	0	2	0	0	0	0	2	2
DL-2-(2,4,5-trichlorophenoxy) propionate	3	0	3	2	2	3	0	0	0	0	0	3[b]	3	0[b]	0[b]	2	0	0	3	0	0	0	0	1	2
2-(α-Terpinyloxyethyl)-*p*-chlorophenoxyacetate	0	0	3	2	3	3	0	0	0	2	0	3[b]	3	0[b]	0[b]	2	0	0	3	0	0	0	0	1	0

[a] Responses observed on 14th day after treatment. 0, no effect; 1, slight effect; 2, moderate effect; 3, marked effect.
[b] Evaluated at 0.1 concentration (equivalent to about 15 γ of test compound per plant; initial concentration, 150 γ per plant, see (*9*) for methods).
[c] Evaluated at 0.01 concentration.

0.67*M*) and 2,4-dichlorophenoxyacetic acid (148 grams, 0.67*M*) were mixed in a flask to which were added 400 ml. of xylene and 2 grams of sulfuric acid. This reaction mixture was refluxed until no more water could be collected in a moisture tube (16 hours). The xylene was removed under reduced pressure yielding a residual heavy oil. Attempts to recrystallize this oil from ethyl acetate and ethyl alcohol were unsuccessful.

The product was effectively extracted batchwise from the oil by hot petroleum ether (boiling point 35° to 59° C.) from which it crystallized on cooling. The crude yield of combined extracts after one recrystallization from petroleum ether was 44.8 grams (20.9%). Two recrystallizations from a mixture of hot ethyl acetate and petroleum ether (boiling point 63° to 70° C.) gave 26.0 grams (yield 12.1%) of purified product melting at 108.5–9.5° C. (Table III).

The other four lactic acid derivatives, DL-2-(2-methyl-4-chlorophenoxyacetoxy) propionic acid methyl and *n*-butyl esters, and DL-2-[DL-2-(2,4,5-trichlorophenoxy) propionoxy] propionic acid methyl and *n*-butyl esters, were prepared by a pyridine catalyzed esterification of the hydroxyl group of the appropriate lactic acid esters. The following example illustrates the procedure.

DL-2-[DL-2-(2,4,5-Trichlorophenoxy)propionoxy]propionic Acid *n*-Butyl Ester. DL-Butyl lactate (52.6 grams, 0.36*M*) was diluted to 500 ml. with a 6 to 1 mixture of petroleum ether (boiling point 63° to 70° C.) and benzene. pyridine (34 ml., 0.42*M*) was added, and the mixture was stirred in an ice bath. The DL-2-(2,4,5-trichlorophenoxy)propionyl chloride (86.4 grams, 0.30*M*), diluted with petroleum ether–benzene mixture, was added dropwise over a 10-minute period. A rapid separation of pyridine hydrochloride indicated an immediate reaction in formation of the product. After 2 hours, the cold reaction mixture was allowed to warm to room temperature. The bulk of the pyridine hydrochloride was removed by filtration and the petroleum ether–benzene solution washed with water, dilute hydrochloric acid, aqueous sodium carbonate, methanol (50%), and water. Following two stages of adsorption treatment with a mixture of sodium sulfate, carbon, diatomaceous earth, and Florisil, the product was vacuum distilled at 187–93° C. at 0.2 mm. of mercury with a constant index of refraction (n_D^{25} = 1.5094). The specific gravity of the product was 1.2679 at 25° C. and the yield was 75%.

Data on the physical properties, yields, and analyses for all the lactic acid derivatives are recorded in Table III.

Methods Used in Plant Tests. The parent and derivatized halogenated phenoxy acids were evaluated for plant growth regulating activity using the dicotyledonous plants, Pinto bean, large seeded sunflower, Arlington White Spine cucumber, and the monocotyledonous plants Wong barley, and U. S.-13 hybrid corn. The lanolin assay method was used on dicots and the coated sand assay method on monocots (*9*).

At intervals of 2, 4, 7, and 14 days following treatment, the degree of growth modification induced by the various compounds was estimated and scored according to the intensity of growth responses. Responses studied were: stem curvature, growth inhibition, epinasty, formative effects, and induced cell proliferation (gall formation). Table IV shows responses observed 14 days after treatment, to conserve space the other values have been omitted. These data are representative, although they do not show the rate of response or relative progressive effectiveness of the compounds tested. The experiments were designed to indicate growth regulating properties rather than the herbicidal potentialities of the compounds.

Results with Plant Tests. In general, coupling of halogenated phenoxy acids with *p*-toluenesulfonamide, *p*-aminobenzoic acid, and *p*-aminosalicylic acid and terpenoids resulted in compounds that induced plant-growth responses, but the magnitude of the different responses was less than that induced by the parent regulating compounds (Table IV). From the standpoint of utilization of these new regulating compounds, the parent phenoxy acids sometimes induce unwanted responses when used for a specific purpose—for example, to improve fruit set. The present data indicate that some derivatives used here may possess limited growth regulating properties of interest. For example, it is desirable to induce fruit set chemically without marked side effects such as modification and suppression of leaf growth. Regulators that induce a localized response are of interest. In the present tests, 2,4,5-trichlorophenoxyacetic acid induced marked responses (formative effects) at a distance from the site of application when applied to bean plants. The hydronopol derivative of this acid, on the other hand, induced a moderate response which was apparently localized within the treated region of the stem.

In a few cases, coupling of the phenoxy acids resulted in compounds with increased growth-regulating properties. When applied to cucumbers, for example, the lactic acid derivative, DL-2-(2 - methyl - 4 - chlorophenoxyacetoxy) propionic acid, methyl ester was more effective than its parent acid, 2-methyl-4-chlorophenoxyacetic acid.

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FRUIT DROP CONTROL

Evaluation of Chlorine-Substituted Phenoxyacetic Acids and Amides for Retarding Abscission of Apple Fruits

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The amide forms of chlorine-substituted phenoxyacetic plant regulators were more effective in retarding mature fruit abscission than the corresponding acids. When chlorine was substituted in all possible combinations on mono-, di-, tri-, tetra-, and penta- positions on the benzene nucleus, in all instances where the 6 position contained chlorine the compound was rated as relatively inactive. To a lesser degree chlorine substitution in the 3 position also reduced the effectiveness of a compound. The 17 acids and 17 amides were compared directly on three varieties of mature apple fruits; the complete series of 17 amides was applied to six varieties.

PLANT-REGULATING ACTIVITIES of chemicals can be compared or evaluated in various ways. Retardation of the abscission of mature fruits of apple was used as the response in the present study, because that type of plant reaction appears to be very different from the cell elongation or multiplication, formative growth effects, parthenocarpy, modification of organs, and repression or stimulation of root or vegetative bud meristems or others (*11*, *15*) commonly used as measures of response.

According to McCown (*4*) the harvest drop of mature apple fruits involves dissolution changes in the walls and lamellae of old, lignified cells. The possible role of plant-regulating chemicals in controlling the metabolism of pectic substances through enzymatic processes has been suggested by Neeley *et al.* (*10*). Other workers have shown that chemical changes associated with the ripening of fruits can be stimulated or